Factors influencing short-term associations between respiratory health and particulate air pollution: Case studies in Asia and Europe in different urban environments

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Zusammenfassung

Zahlreiche Studien belegen schädigende Assoziationen zwischen Atemwegserkrankungen und gasförmigen und partikulären Luftschadstoffen. Feinstaub erwies sich als besonders schädigend. Es ist jedoch noch nicht geklärt, welche Partikelfraktionen des Feinstaubes für die Zusammenhänge verantwortlich sind.

In dieser Arbeit werden die Kurzzeit-Effekte von grobem Feinstaub (TSP) sowie den gasförmigen Schadstoffen Schwefeldioxid (SO_2) und Stickstoffdioxid (NO_2) auf Krankenhauseinweisungen aufgrund von Atemwegserkrankungen in Drobeta, Rumänien untersucht. Zudem wird der Zusammenhang von PM_{10} (Partikel mit einem Durchmesser $< 10\,\mu m$), NO_2, SO_2 und größenabhängigen Partikelanzahlkonzentrationen (PNC) mit respiratorischen Notfallaufnahmen und Sterbefällen in Peking, China, analysiert. Für Peking wird zudem ein statistisches Modell entwickelt, um fehlende PNC zu modellieren. Ziel der Arbeit ist es, die relevanten Faktoren in den Beziehungen zwischen Atemwegserkrankungen und Luftverschmutzung, vor allem Feinstaub, zu untersuchen.

In beiden Städten wurde ein schädigender Einfluss von Luftschadstoffen auf Atemwegserkrankungen festgestellt. In Drobeta waren TSP und SO_2 mit Atemwegserkrankungen assoziiert, wobei der schädigende Einfluss von TSP durch trockene Luft verstärkt wurde. In Peking zeigten vor allem Akkumulationspartikel (Durchmesser $0.1 – 1\,\mu m$) eine schädigende Wirkung, welche für ultrafeine Partikel (UFP, < 100 nm) nicht festgestellt werden konnte. Dabei war der Einfluss von PNC unabhängig von PM_{10}. Der Effekt von PNC war für stagnierende Luftmassen größer, was darauf hinweist, dass neben der Partikelanzahl und -oberfläche die Partikelchemie einen negativen Einfluss hat. Darüber hinaus wurde eine Assoziation von NO_2 mit Notfallaufnahmen und von SO_2 mit der Mortalität festgestellt.

Die Ergebnisse bestätigen den schädigenden Einfluss von gasförmigen sowie partikulären Luftschadstoffen auf Atemwegserkrankungen und weisen auf größenabhängige Effekte von Feinstaub hin.

Abstract

Numerous epidemiological studies have described adverse effects of particulate and gaseous air pollution on respiratory health. Especially particulate matter (PM) seems to be relevant for the observed associations. However, it is not yet clear which particle fractions are responsible for the observed health effects of PM.

In the presented studies, we analyse the short-term associations of total suspended particles (TSP) as well as of sulphur dioxide (SO_2) and nitrogen dioxide (NO_2) with respiratory hospital admissions in Drobeta, Romania. Moreover, effects of PM_{10} (PM with a diameter < 10 µm), NO_2, SO_2, and size-segregated particle number concentrations (PNC) on respiratory mortality and emergency room visits (ERV) are investigated for Beijing, China. For Beijing, we also develop a statistical model to impute missing PNC. The aim of the studies is to investigate the factors influencing the short term associations between respiratory health and air pollution, especially PM.

Air pollution was adversely associated with respiratory health in Drobeta and Beijing. In Drobeta, TSP and SO_2 were adversely associated with hospital admissions for chronic bronchitis; thereby, dry air aggravated the adverse associations of TSP. In Beijing, mostly accumulation mode particles (0.1 – 1 µm) showed adverse associations with respiratory health, whereas, there was a lack thereof for ultrafine particles (UFP). The effects of PNC were found to be independent of PM_{10}. Adverse health effects of PNC were stronger for stagnant air masses indicating that, besides particle number and surface area, also particle chemistry influences the observed associations, as stagnant air masses result in chemically diverse particles. Also, NO_2 was adversely associated with respiratory ERV and SO_2 with respiratory mortality.

These findings underline the strong influence of gaseous and particulate air pollution on respiratory health and indicate size dependent effects of particulate matter.

Schlagwörter

Luftverschmutzung, Feinstaub, Erkrankungen der Atemwege, Zeitreihenanalyse, größenabhängige Partikelanzahl

Keywords

Air pollution, Particulate Matter, Respiratory diseases, Time-series analyses, Size-segregated particle numbers

Inhaltsverzeichnis

Abkürzungsverzeichnis

CEE	Central Eastern Europe
CI	Confidence interval
CB	Chronic bronchitis
COPD	Chronic obstructive pulmonary disease
ERV	Emergency room visits
GAM	Generalized additive model
IQR	Interquartile range
NO_2	Nitrogen dioxide
PDLM	Polynomial distributed lag model
PEF	Peak expiratory flow
PM	Particulate matter
PM_{10}	Particle mass of particles with an aerodynamic diameter < 10 µm
$PM_{2.5}$	Particle mass of particles with an aerodynamic diameter < 2.5 µm
PNC	Particle number concentration
PNC_x	Particle number concentration in the given (x in nm) or total size range (3 nm - 1 µm)
PSC_x	Particle surface area concentration in the given (x in nm) or total size range (3 nm - 1 m)
r	Pearson's correlation coefficient
RR	Relative risk
SO2	Sulfur dioxide
TSP	Total suspended particles
UFP	Ultrafine particles - Particles with an aerodynamic diameter < 100 nm
WHO	World Health Organization

Vorwort

Die vorliegende kumulative Dissertation entstand im Rahmen meiner Zeit als Promotionsstudent am Helmholtzzentrum für Umweltforschung – UFZ in der „Core Facility Studien“ im Rahmen des DFG-Projektes FR-1417/3-2 „Short-Term Health Effects of Fine and Ultra Fine Particle Pollution in Beijing, China“. Im Folgenden sind die aufgedeckten Zusammenhänge zwischen Luftverschmutzung, vor allem Feinstaub, und Erkrankungen der Atemwege zusammengefasst.

Im ersten Kapitel werden Hintergrundinformationen über den Zusammenhang zwischen Luftschadstoffen und Atemwegserkrankungen dargestellt. Die Kapitel zwei bis fünf bestehen aus einem eingereichten, einem zur Publizierung freigegeben und zwei publizierten Arbeiten. Aus Urheberrechtsgründen sind jedoch nur die Abstracts und nicht die kompletten Artikel enthalten. Im sechsten beziehungsweise letzten Kapitel werden die Ergebnisse zusammengefasst und in einen größeren wissenschaftlichen Zusammenhang gestellt.

Eingereichte Arbeiten:

Leitte, A.M., Herbarth, O., Wichmann, H.E., Pan, X.-C., Hu, M., Wiedensohler, A., Schlink, U., Wehner, B., Tuch, T., Wu, Z., Liu, L., Breitner, S., Cyrys, J., Peters, A., & Franck, U. (Submitted). Modelling daily size segregated particle number concentrations for a possible later use in epidemiological time series analyses - A case study for Beijing.

Leitte, A.M., Petrescu, C., Franck, U., Richter, M., Suciu, O., Ionovici, R., Herbarth, O., & Schlink, U. (2009). Respiratory health, effects of ambient air pollution and its modification by air humidity in Drobeta-Turnu Severin, Romania. Science of the Total Environment, 407, 4004-4011.

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1 Introduction

The air we breathe is a mixture primarily of the gases nitrogen (~ 78 %) and oxygen (~ 21 %), but there are also traces of other gases, water vapour, and possibly air pollutants (Seinfeld and Pandis 1996). Air pollutants affect different areas and are contaminants in the atmosphere such as dust, fumes, gases, mist, odour, smoke, or vapour in quantities and of characteristics and duration such as to be injurious to human, plant, or animal life or to property, or to interfere unreasonably with the comfortable enjoyment of life and property (Lapedes 2003).

Human health effects of air pollution have been analysed systematically since the beginning of the 20th century, after severe air pollution episodes from industrialised processes resulted in health problems in the Meuse valley in Belgium (Nemery et al. 2001) and in London, Great Britain (Whittaker et al. 2004). Hence, numerous epidemiological studies have been conducted worldwide to understand the associations between air pollution and human health in order to protect public health. Epidemiological studies are crucial for assessing effects directly in humans and estimating risks for populations, whereas toxicological studies elucidate underlying causal mechanisms (Pershagen 1999). Studies have investigated the associations between air pollution and prenatal associations, brain development, allergic reaction, and other aspects of human health. Most studies, however, have focused on the cardiovascular and respiratory system. The burden of air pollution on human health is high. The estimated health costs of air pollution in China were about 65 billion dollar or 3.8 % of the country's gross domestic product in 2003 (World Bank 2007), and air pollution is estimated to cause approximately two million premature deaths worldwide per year (WHO 2005a).

Particulates or particulate matter (PM), which is a part of air pollution, is a complex mixture of solid and liquid particles suspended in the air that arises directly from emissions and from the conversion of some gases (Seinfeld and Pandis 1996). Among other air pollutants, PM is regarded as a major threat to human health (WHO 2005a). Many authorities set up air quality standards for air pollutants, including PM, in order to protect public health. Particulate air quality standards refer to measurements of mass concentrations of PM with an aerodynamic diameter < 10 µm (PM_{10}), $PM_{2.5}$ (PM with an aerodynamic diameter < 2.5 µm) and TSP (total suspended particulates) that also include particles > 10 µm. Most epidemiological studies about the health effects of PM use particle mass as exposure. Seaton et al. (1995) were one of the first who proposed that high particle number concentrations (PNC) are highly responsible for the observed health effects due to particulate air pollution. Many toxicological studies have elucidated casual mechanisms between PNC and respiratory health outcomes. Small particles that are best represented by PNC may contribute to the health effects of PM because of their high number, high deposition rate in the respiratory tract, ability to evade macrophage phagocytosis, and high surface area resulting in a potential high inflammatory and oxidant stress (Oberdörster et al. 2005; Terzano et al. 2010).

Most studies have been conducted in North America and Western Europe. However, their results might not be transferable to other regions due to differences in population, health care, levels and composition of air pollution, climate, and other factors. Moreover, it is not yet clear which particle characteristics describe the health effects best.

Epidemiological time series studies on the associations between respiratory health and size-segregated PNC are rare, as the necessary long-term measurements of at least one year length of PNC has been available just since recent years. Moreover, most studies that have been conducted so far concentrate solely on Western Europe, but findings from these studies are not consistent. Two studies conducted in Germany and Finland, for example, observed an adverse influence of ultrafine particles (UFP) on peak expiratory flow (PEF) (Peters et al. 1997; Penttinen et al. 2001). PEF quantifies the ability to breathe out air by measuring the maximum flow which is generated during expiration with maximal force. Another study conducted in Finland did not observe stronger associations of UFP with variations in PEF than with PM_{10} or black smoke (BS) (Pekkanen et al. 1997). In contrast, Osunsanya et al. (2001) observed no associations between UFP and PEF in Aberdeen, Scotland.

In Copenhagen, Denmark, the adverse health effects of PM on respiratory hospital admissions among the elderly were mainly mediated by PM_{10} and accumulation mode particles with lack of effects for UFP, whereas for paediatric asthma, accumulation mode particles and UFP were relevant and PM_{10} appeared to have little effect (Andersen et al. 2008). Total PNC were adversely associated with all-cause and cardiovascular mortality and cardiovascular hospital admissions in London, Great Britain, but not with respiratory outcomes. These were associated with secondary pollutants, especially non-primary $PM_{2.5}$ (Atkinson et al. 2010). Braniš et al. (2010) observed adverse associations between different fractions of PNC and hospital admissions due to cardiovascular and respiratory diseases, but no associations for mortality in Prague, Czech Republic. In Helsinki, Finland, nucleation mode (< 0.03 µm), Aitken mode (0.03 – 0.1 µm) and accumulation (0.1 – 0.29 µm) mode particles, all with a lag of 3 to 5 days, were adversely associated with asthma visits of children, but only accumulation mode and coarse particles (2.5 – 10 µm) were associated with asthma and COPD among adults (Halonen et al. 2008). Also in Helsinki, Aitken mode, accumulation mode, and coarse mode particles had adverse respiratory health effects among the elderly (Halonen et al. 2009). Mortality, including respiratory mortality, was consistently adversely associated with PNC, especially for cumulative exposures of UFP in Erfurt, Germany (Wichmann et al. 2000; Stölzel et al. 2007; Breitner et al. 2009).

The aim of the studies presented in this thesis was to analyse the associations between particulate air pollution and respiratory health, and factors influencing these associations. We focused on locations in Eastern Europe (Drobeta, Romania) and Asia (Beijing, China).

Especially in Romania epidemiological analyses about air pollution and health are rare. We investigated the associations between respiratory hospital admissions and air pollution (TSP, sulphate (SO_2), and nitrate (NO_2)) in Drobeta-Turnu Severin (Leitte et al. 2009). Drobeta-Turnu Severin has a population of approximately 100,000 people and is situated in the south-western part of Romania. The levels of air pollution are influenced by local heavy industry, and the climate is temperate and continental with cold winters and warm summers. In addition, the modification of the associations of TSP by air humidity was investigated in Drobeta-Turnu Severin (Leitte et al. 2009).

Furthermore, we analysed the associations between size-segregated PNC and respiratory health in Beijing China. The population of Beijing, the capital of China, in 2005 was ~ 15 million inhabitants (Beijing Municipal Bureau of Statistics 2006) and 8 million people living in the urban area. The climate is humid continental with dry winters and warm summers. Air pollution is heavy due to abundant local and surrounding sources (Chan and Yao 2008). We obtained time series of size-segregated PNC from an urban background measurement station in Beijing, China, from the Leibniz Institute for Tropospheric Research (IfT). Data were available in the following size classes: 3 – 10 nm (PNC_{3-10}), 10 – 30 nm (PNC_{10-30}), 30 – 50 nm (PNC_{30-50}), 50 – 100 nm (PNC_{50-100}), 100 – 300 nm ($PNC_{100-300}$), 300 – 1000 nm ($PNC_{300-1000}$), 3 – 100 nm (UFP), and 3 – 1000 nm (PNC_{tot}). Additionally, we gathered meteorological data from a background measurement station and air pollution data (PM_{10}, SO_2, and NO_2) as an urban average. We then analysed the associations of air pollution, especially size-segregated PNC with respiratory morbidity (Leitte et al. 2010) and mortality (Leitte et al. Accepted) in Beijing. Time series of PNC normally contain gaps due to maintenance or failure of measurement devices. PNC were shown to be related to weather conditions (Wehner et al. 2008; Wu et al. 2008). Thus, we also developed a statistical model to impute missing values. We created artificial gaps in modelled PNC and made a comparison between modelled and measured PNC and compared health effects of predicted and measured PNC. We showed that is an adequate approach to model PNC on a daily basis for the later use in epidemiological time series analyses (Leitte et al. Submitted).

The aim of the studies was to analyse the factors influencing short-term associations between respiratory health and particulate air pollution and to answer the following questions: Which particle size fractions are the most harmful for human respiratory health? Which of the particle size fractions describe the health effects best? Which role do the recently often discussed UFP play in the observed associations? Are the associations of particulate matter independent of other air pollutants? What role do particle numbers and mass play in the observed health effects of particulate matter? Which sources are related to the air pollutants associated with respiratory health?

2 Size-Segregated Particle Number Concentrations and Respiratory Emergency Room Visits in Beijing, China

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Leitte, A.M., Schlink, U., Herbarth, O., Wiedensohler, A., Pan, X.-C., Hu, M., Richter, M., Wehner, B., Tuch, T., Wu, Z., Yang, M., Liu, L., Breitner, S., Cyrys, J., Peters, A., Wichmann, H.E., & Franck, U. (2010). Size-Segregated Particle Number Concentrations and Respiratory Emergency Room Visits in Beijing, China. Environmental Health Perspectives, 119, 508-513.

Abstract

Background: The link between concentrations of particulate matter (PM) and respiratory morbidity has been investigated in numerous studies.

Objectives: The aim of this study was to analyze the role of different particle size fractions with respect to respiratory health in Beijing, China.

Methods: Data on particle size distributions from 3 nm to 1 µm; PM_{10} (PM ≤ 10 µm), nitrogen dioxide (NO_2), and sulfur dioxide concentrations; and meteorologic variables were collected daily from March 2004 to December 2006. Concurrently, daily counts of emergency room visits (ERV) for respiratory diseases were obtained from the Peking University Third Hospital. We estimated pollutant effects in single- and two-pollutant generalized additive models, controlling for meteorologic and other time-varying covariates. Time-delayed associations were estimated using polynomial distributed lag, cumulative effects, and single lag models.

Results: Associations of respiratory ERV with NO_2 concentrations and 100 – 1000 nm particle number or surface area concentrations were of similar magnitude – that is, approximately 5 % increase in respiratory ERV with an interquartile range increase in air pollution concentration. In general, particles < 50 nm were not positively associated with ERV, whereas particles 50 – 100 nm were adversely associated with respiratory ERV, both being fractions of ultrafine particles. Effect estimates from two-pollutant models were most consistent for NO_2.

Conclusions: Present levels of air pollution in Beijing were adversely associated with respiratory ERV. NO_2 concentrations seemed to be a better surrogate for evaluating overall respiratory

3 Modelling daily size segregated particle number concentrations for a possible later use in epidemiological time series analyses - A case study for Beijing

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Leitte, A.M., Herbarth, O., Wichmann, H.E., Pan, X.-C., Hu, M., Wiedensohler, A., Schlink, U., Wehner, B., Tuch, T., Wu, Z., Liu, L., Breitner, S., Cyrys, J., Peters, A., & Franck, U. (Submitted). Modelling daily size segregated particle number concentrations for a possible later use in epidemiological time series analyses - A case study for Beijing.

Abstract

Background: There is still lack of knowledge about particle size and the associated health effects. Maintenance and breakdown of measurement devices often result in gaps of time series of size-segregated particle number concentrations (PNC). Thus, reliable imputing methods are required. The aim of this study was imputing gaps in time series of daily PNC in the size range from 3 nm to 10 µm for a possible later use in epidemiological time series analyses.

Methods: We collected daily mean values of size segregated PNC, other air pollutants (PM_{10}, NO_2, and SO_2), and meteorological variables from 2004 to December 2006 in Beijing, China. Feed forward neural networks were used to model daily mean values of size segregated PNC. We evaluated the accuracy of predicted PNC and compared health effect estimates using observed and modelled PNC.

Results: Descriptive statistical parameters of daily PNC were similar for observed and predicted data. The correlation between observed and predicted PNC was moderate to high ($0.59 < r < 0.85$). Measures of error showed a good agreement between predicted and observed PNC in the size range 3 – 10 nm and 100 – 1000 nm. Associations between respiratory health and PNC with observed and predicted values had the same tendency with respect to health effects, i.e. 85 % of the adverse associations for observed PNC were also adverse for predicted PNC and the same for protective associations. The percentage difference of associations (RR) was smaller 5%.

Conclusions: Statistical models can be applied to estimate size segregated particle number concentrations on a daily basis. Imputed time series of PNC, especially in the size range 3 – 30 nm and 100 – 1000 nm, might be used in epidemiological time series analyses.

4 Associations between Size Segregated Particle Number Concentrations and Respiratory Mortality in Beijing, China

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Leitte, A.M., Schlink, U., Herbarth, O., Wiedensohler, A., Pan, X.-C., Hu, M., Wehner, B., Breitner, S., Peters, A., Wichmann, H.E., & Franck, U. (19 Aug 2011, Epub ahead of print). Associations between Size Segregated Particle Number Concentrations and Respiratory Mortality in Beijing, China. DOI:10.1080/09603123.2011.605878 International Journal of Environmental Health Research.

Abstract

Introduction: Numerous studies have described the adverse associations between particle mass and respiratory health. The aim of the study was to analyse the associations of particle properties, especially size segregate particle number concentrations (PNC), and respiratory mortality in Beijing, China.

Methods: We gathered daily values of respiratory mortality and air pollution data of the Beijing urban area. Generalized additive models were used to estimate the associations.

Results: Single pollutant models showed that delayed concentrations of SO_2, total PNC, and PNC of 300 – 1000 nm were adversely associated with total respiratory mortality. There was an indication that adverse health effects of PNC might be stronger for stagnant air masses. Two-pollutant models verified the independence of associations of total PNC of other pollutants (SO_2, NO_2, and PM_{10}).

Conclusions: Particle number concentrations, especially accumulation mode particles, might be factors influencing the adverse associations between particulate matter and respiratory health.

5 Respiratory health, effects of ambient air pollution and its modification by air humidity in Drobeta-Turnu Severin, Romania

This article has been published in the journal "Science of the Total Environment".

Leitte, A.M., Petrescu, C., Franck, U., Richter, M., Suciu, O., Ionovici, R., Herbarth, O., & Schlink, U. (2009). Respiratory health, effects of ambient air pollution and its modification by air humidity in Drobeta-Turnu Severin, Romania. Science of the Total Environment, 407, 4004-4011.

Abstract

Background: Associations between ambient air pollution and respiratory health have been mainly reported for Western Europe and Northern America. Objectives: Our goal was to investigate such associations among the population of Drobeta-Turnu Severin, Romania, a city in Central Eastern Europe (CEE), and to quantify their modification by air humidity. The latter is of increased interest for the current discussion about the potential effects of climate change on human health.

Methods: We investigated (study period: 23.01.2001 – 31.08.2002) the associations between chronic obstructive pulmonary disease (COPD), asthma and chronic bronchitis (CB) and total suspended particles (TSP), sulphur dioxide (SO_2) and nitrogen dioxide (NO_2). Generalized additive models (GAM) controlling for time patterns and weather effects were applied. Delayed effects up to seven days were analysed in single lag and polynomial distributed lag models (PDLMs).

Results: An increase of 10 $\mu g/m^3$ TSP was related to a 3.3 % (95 % CI: 0.3 – 6.4 %) and a 2.8 % (95 % CI: 0.1 – 5.7 %) increase for hospital admissions for chronic bronchitis with a lag of one and four days, respectively. The adverse effect of TSP on chronic bronchitis was reduced by higher humidity. An increase of 10 $\mu g/m^3$ SO_2 was related to a 6 % (95 % CI: 7 – 25 %) increase, with a two days lag, for hospital admissions for chronic bronchitis. We have not been able to identify a threshold, below which ambient TSP and SO_2 concentrations have no effect on hospital admissions for chronic bronchitis. We found adverse but not significant influences of TSP, SO_2 and NO_2 on total respiratory hospital admissions, COPD and asthma and NO_2 on chronic bronchitis.

Conclusions: We conclude that in Drobeta-Turnu Severin CB is associated with TSP and mainly SO_2. Dry air aggravates the adverse effect of TSP.

6 Summary and Discussion of Results

In the following, a summary and discussion of the results of the four publications about the associations between air pollution and respiratory health in Beijing, China and Drobeta, Romania are presented.

6.1 Descriptive results

First, a statistical description of the air pollution and health data for both cities is given.

6.1.1 Air pollution data

Air pollution in Beijing is very high (Chan and Yao 2008) and is ranked to be one of the worst in the world (Gurjar et al. 2008). In the period March 2004 to December 2006, the mean mass concentration of PM_{10} was 120 µg/m³. The European air quality standards (2008/50/EC) for PM_{10} impose an annual average concentration value of 40 µg/m³ and a daily concentration value of 50 µg/m³ which must not be exceeded more than 35 times per calendar year. PM_{10} concentrations in Beijing were 3 times higher than the annual European air quality standard and daily mean concentrations exceeded 50 µg/m³ of PM_{10} in most cases (874 of 1036 days). The mean of total PNC in Beijing was 30,000 1/cm³, and thus, about 30 % higher than in European cities (Wehner et al. 2008). Mean concentrations in the period March 2004 to December 2006 of SO_2 (87 µg/m³) and NO_2 (63 µg/m³) exceeded the Chinese secondary ambient air quality standards for SO_2 (60 µg/m³) and NO_2 (40 µg/m³). Chinese secondary air quality standards that are based on daily mean concentrations (SO_2: 150 µg/m³, NO_2: 80 µg/m³, and PM_{10}: 150 µg/m³) are higher than European limit values, but were exceed several times (SO_2:153 times, NO_2: 232 times, and PM_{10}: 258 times out of 1036 days) in the study period. Based on a quantitative comparison of different air pollution concentrations the Air Pollution Index of Beijing indicates that air pollution is often determined by PM_{10} (Chan and Yao 2008). There are abundant and diverse sources of air pollution in Beijing and the most important are power plants, domestic heating, and industrial, vehicular, biogenic, and non local sources (Chan and Yao 2008).

PNC were dominated by particles < 0.3 µm, particle surface area concentrations (PSC) by particles in the range of 0.05 – 1 µm, and particle volume or mass concentration by particles in the range 0.1 – 10 µm. Correlations between adjacent fractions of PNC were moderate to high (> 0.55), and total PNC was low to moderately correlated ($|r| > 0.15$) with meteorological (air temperature, relative air humidity and air pressure) and other air pollutant (SO_2, NO_2 and PM_{10}) variables. PNC of particles < 30 nm and > 100 nm were negatively correlated. The high particles' surface area encountered in the Beijing atmosphere acts as an effective coagulation sink for nucleation mode particles (Wehner et al. 2008). Nucleation, i.e. the formation of new particles resulting in high concentrations of small particles (< 30 nm), are not limited by gaseous precursor concentrations but rather the pre-existing larger particles that act as the coagulation sink.

In Drobeta, the mean concentration of TSP was 123 µg/m³. Assuming that TSP consists to 60 % of PM_{10}, which is in agreement with other studies (Brook et al. 1997; Chen and Mao 1998; Fang et al. 1999; Mugica et al. 2002) the annual European threshold of 40 µg/m³ PM_{10} was exceeded by 33 µg/m³ PM_{10} and the European daily threshold of 50 µg/m³ was exceeded on 457 out of 586 days, indicating that particulate air pollution was high in Drobeta. Mean concentrations of SO_2 and NO_2 were moderate to low (SO_2: 5 µg/m³ and NO_2: 12 µg/m³). Main sources of air pollution were a paper plant, different thermal power stations, and other heavy industries. Interestingly, the correlation between TSP and SO_2 and NO_2 was low.

6.1.2 Mortality and Morbidity Data

All time series of respiratory health in Beijing and Drobeta contain seasonal cycles. Additionally, hospital admissions in Beijing and Drobeta contain a weekly pattern which was a result of the hospital management. In Beijing, most counts of total respiratory (J00 – J99) emergency room visits (n = 15,981) were due to acute respiratory diseases (J00 – J09), and in case of mortality (n = 3528) due to chronic diseases (J40 – J47). Cases of respiratory health in Drobeta-Turnu Severin (n = 1529) were most frequent due to COPD, followed by asthma and chronic bronchitis.

6.2 Associations between air pollution and respiratory health

After controlling for confounding effects, we computed associations between air pollution and respiratory health. Different pollutants and health outcomes were studied in the two study areas. Thus, direct comparisons between the two cities were in most cases not possible. Moreover, it has been suggested that pollutants might be better interpreted as indicators of the biologically relevant pollution mixture and that the indicators might vary with location (Sarnat et al. 2001) which renders the direct comparisons of pollutants in different cities a less suitable strategy.

6.2.1 Gaseous air pollution

We observed adverse associations between respiratory health and gaseous air pollution (SO_2 and NO_2) in both study areas. Adverse associations between air pollution including gaseous pollutants and respiratory health have been reported in the literature (Perez et al. 2010). Hospital admissions for chronic bronchitis increased by approximately 10 % for an increment of 1 µg/m^3 SO_2 with a delay of 2 and 7 days in Drobeta. SO_2 is an invisible gas and its anthropogenic source is mainly industrial activity where materials containing sulphur are processed such as during the generation of electricity from coal or oil. The effect estimate of SO_2 is rather high compared to values in the literature (Wilson et al. 2005). Nevertheless, the maximum SO_2 concentrations observed in Drobeta resulted in a lower increase in hospital admissions for chronic bronchitis compared to the maximum observed level of TSP, with reference to absolute clean air conditions. In a multi-pollutant model including all adverse single pollutant effects of SO_2 and TSP, the effect of SO_2 with a delay of two days remained. This could be explained by a more important influence of SO_2 on chronic bronchitis than of TSP, as observed by Herbarth et al. (2001).

In Beijing, we observed that SO_2 was adversely associated with respiratory mortality. The increase in total respiratory mortality was about 2.73 % for an IQR increment in SO_2 (44 µg/m³) as a lagged average of four and five days. In a meta-analysis of the association between air pollution and mortality based on results of time-series studies published since 1985 an increment in 10 µg/m³ SO_2 has been reported to be associated with a 0.36 % increase in mortality (Stieb et al. 2002). The effect estimate is based on 46 studies and effect estimates for cause-specific mortality due to respiratory diseases are higher. Based on a systematic review and meta-analysis of 7 epidemiological time-series studies on outdoor air pollution and health in Asia, a 1 % increase in respiratory mortality resulted from a 10 µg/m³ SO_2 increment (Atkinson et al. 2011). Our observed effect estimate is slightly higher but of comparable magnitude to other effect estimates about the association between SO_2 and respiratory mortality reported in the literature.

In our two-pollutant models, effect estimates as a lagged SO_2 average of four and five days were slightly lower in magnitude when controlling for PM_{10} ($p < 0.046$) or PNC ($p < 0.063$), and lower and non-significant when controlling for NO_2. In other Chinese studies (Xu et al. 1994; Chen et al. 2008), effects of SO_2 on mortality were also independent of PM_{10}. Main sources of SO_2 in Beijing are domestic heating, power plants and industrial sources (Meng et al. 2008) which are similar to PM_{10} sources. Sulphur acid, resulting from oxidation of SO_2 was shown to be a dominant factor in new particle formation, but also in the subsequent growth of particles in Beijing (Yue et al. 2010). We cannot conclude that our observed health effects are attributable to SO_2 or are a proxy for other pollutants like PNC. Based on our findings, we conclude, that the biologically relevant air pollution mixture in Beijing contains air pollutants that are in relation to sulphate.

NO_2 was adversely associated with total respiratory ERV in Beijing which is in agreement with other studies (Peel et al. 2005; Tolbert et al. 2007; Stieb et al. 2009). Respiratory ERV increased by 6.1 % (95 % CI: 0.0 % to 12.5 %) with an IQR increment (40 µg/m³) in NO_2 with a one day lag. In two-pollutant models, associations between respiratory ERV and NO_2 were more consistent than those for other pollutants and effect estimates of NO_2 were higher in magnitude after adjustment for PM_{10}. NO_2 itself has adverse health effects at high concentrations (> 200 µg/m³) (WHO 2005a), but such levels have only occurred on 11 days during the study period in Beijing. Main sources of NO_2 are traffic and other combustion processes, which are major sources of air pollution in general and of particles in Beijing (Sun et al. 2004). Traffic-related air pollution has been associated with respiratory diseases in several studies (Bayer-Oglesby et al. 2006; Brunekreef et al. 2009; Hazenkamp-von Arx et al. 2011). In two-pollutant models associations with NO_2 were most consistent. A pollutant which exhibits a relatively strong association in a multi-pollutant model may be acting as a surrogate for an unmeasured or poorly measured pollutant (Peel et al. 2005). Thus, it might be possible that our observed adverse associations for NO_2 were due to NO_2-correlated air pollution. We hypothesize that the biologically relevant pollution mixture was traffic-related air pollution and was most important for the observed adverse association with respiratory ERV in Beijing China.

6.2.2 Particle Mass

In our studies particle mass (PM_{10} and TSP) was associated with respiratory outcomes. For TSP in Drobeta, an increment in 10 µg/m³ TSP was associated with a 3.3 % (95 % CI: 0.3 % to 6.4 %) and 2.8 % (95 % CI: 0.1 % to 5.7 %) increase in hospital admissions of chronic bronchitis with a lag of one and four days, respectively. TSP include particles > 10 µm and therefore might be regarded as a surrogate for coarse particle mass concentration. In the literature coarse particles are referred to PM in the size range 2.5 to 10 µm, and effects of coarse particles and respiratory health might be independent of the effects of fine particles (Brunekreef and Forsberg 2005).

When assuming that TSP consists to 60 % of PM_{10} (World Bank 2001), a 10 µg/m³ increment in PM_{10} converted from TSP would result in a 1.8 % increase in hospital admissions for chronic bronchitis. In Beijing, respiratory ERV increased by 0.12 % (95 % CI: –0.27 % to 1.51 %) and 0.03 % (95 % CI: –0.62 % to 0.71 %) for an elevation of 10 µg/m³ PM_{10} of the same day and as an average of same day and five previous days, respectively. Worldwide, several studies analysed the short-term associations between respiratory health and particle mass concentrations. A World Health Organization (WHO) meta-analysis of peer reviewed European studies has provided a summary estimate of a 0.8 % increase in respiratory ERV for an increment in 10 µg/m³ PM_{10} (Anderson et al. 2004). A meta-analysis of exposure-response coefficients for health effects due to air pollution based on Chinese epidemiological studies has reported an increase of 1.2 % in respiratory hospital admissions for a 10 µg/m³ PM_{10} increment (Aunan and Pan 2004). Compared to the literature, our observed associations were of comparable magnitude, slightly lower in Beijing and slightly higher in Drobeta.

Additionally, we observed an increase of 0.03 % (95 % CI: –0.43 % to 0.52 %) and 0.48 % (95 % CI: –0.23 % to 1.25 %) in total respiratory mortality in Beijing for an increment in 10 µg/m³ PM_{10} of the same day and as an average of same day and five previous days, respectively. In Europe, an increment of 10 µg/m³ PM_{10} was related to a 1.3 % increase in respiratory mortality (Anderson et al. 2004), whereas in China the effect estimate is reported to be 0.6 % (Aunan and Pan 2004).

Overall, we observed significant adverse associations between disease-specific respiratory health and TSP in Drobeta, whereas we observed adverse but non-significant associations for all respiratory health in Drobeta and Beijing. The values of our observed associations were in the range of a 0.03 to 1.8 % increase in respiratory health for a PM_{10} increment of 10 µg/m³. Associations between respiratory health (mortality and morbidity) and PM_{10}, also for a 10 µg/m³ increment, have been reported to be in the range of 0.6 to 1.3 % in Western and Asian countries (Anderson et al. 2004; Aunan and Pan 2004) and are of similar magnitude compared to our observed associations. This supports the finding of the WHO that the health risks for PM_{10} are likely to be similar in cities in developed and underdeveloped countries (WHO 2005b).

6.2.3 Size segregated particle number concentrations

6.2.3.1 Respiratory ERV

We observed adverse associations between size-segregated PNC and respiratory health in Beijing. For total PNC we observed adverse associations which were strongest on the same day or with a delay of 2 days, but for a delay of 4 days the association was protective. Particles can be categorized by size into the following classes: nucleation particles (3 – 30 nm), Aitken particles (30 – 100 nm), ultrafine particles (3 – 100 nm), and accumulation particles (100 – 300 nm and 300 – 1000 nm). Accumulation particles showed the strongest effects on respiratory ERV. We observed an increase of 5 % (95 % CI: 2 % to 8 %) for an IQR increase (4,400 cm^{-3}) in $PNC_{100\text{-}300}$ with a one day lag. Accumulation mode particles are directly emitted by combustion processes or formed by coagulation of smaller particles and by the heterogeneous condensation of gas vapour onto existing aerosol particles (Seinfeld and Pandis 1996). Removal mechanisms of accumulation mode particles are least efficient, causing particles to accumulate in the atmosphere (Seinfeld and Pandis 1996). Adverse associations for an IQR increment in PNC of 100 – 300 nm and 300 – 1000 nm particles were of similar magnitude and resulted in an approximately 5 – 8 % increase in respiratory ERV. Few other studies have reported similar findings. In agreement to our study, accumulation particles had the strongest effect on hospital admissions for cardiovascular and respiratory diseases among size-resolved PNC in Prague, Czech Republic (Braniš et al. 2010). Results from Helsinki, Finland, also indicated that accumulation mode particles play an important role in the associations with respiratory hospital admissions. Halonen et al. (Halonen et al. 2009) reported that strongest and most consistent associations with acute respiratory hospital admissions among the elderly (> 64 yrs) were found for an IQR increment in accumulation mode particles as a 5-day mean 3.1 % (95 % CI: 0.43 % to 5.8 %) for pneumonia and for the same day 3.8 % (95 % CI: 1.3 % to 6.3 %) for pooled asthma COPD. In addition, pooled asthma COPD hospital emergency room visits for adults (15 – 64 yrs) and asthma visits for children (< 15 yrs) increased by ~ 3 % for an IQR increment in accumulation mode particles (Halonen et al. 2008). Further evidence of the adverse influence of accumulation mode particles comes from a study conducted in Copenhagen, Denmark (Andersen et al. 2008), where an IQR increment in accumulation mode particles was associated with an increase in respiratory hospital admissions for the elderly [4 % (95 % CI: 1 % to 8 %)] and in paediatric asthma [8 % (95 % CI: 0 % to 17 %)]. Reported effect estimates of an approximately 5 % increase in respiratory health for an IQR increment in accumulation mode particles are in good agreement to our observed associations for $PNC_{100\text{-}300}$ and $PNC_{300\text{-}1000}$. Results from our studies add supporting information that accumulation mode particles are a relevant fraction for associations with respiratory health. All comparable studies have been conducted in Western Europe; such an analysis has not been done before in Beijing, China.

In two-pollutant models with control for NO_2, associations of PNC and PSC remained in its magnitude, and associations of $PNC_{100-300}$ and $PSC_{100-300}$ as the mean of three days (present and previous two days) were moderately significant ($p < 0.09$). As mentioned earlier, a pollutant - in this case NO_2 - that is strongly associated in a multi-pollutant model may be acting as a surrogate for an unmeasured or poorly measured pollutant (Peel et al. 2005). We already discussed adverse associations between NO_2 and respiratory ERV in Beijing above. NO_2 was moderately correlated ($0.42 < r < 0.59$) with particle number and surface area concentrations of fractions > 50 nm and total PSC. Sources of NO_2 and particles > 50 nm mainly are combustion processes, especially traffic. This gives further evidence that traffic-related air pollution has a strong influence on respiratory health in Beijing. Traffic-related air pollution has been shown to be related to several health outcomes including respiratory diseases (de Kok et al. 2006; Brunekreef et al. 2009).

In single pollutant models we observed adverse, yet non-significant associations between respiratory ERV and PM_{10}. The associations between respiratory ERV and particle number and surface area concentrations remained adverse and were slightly higher when controlling for particle mass concentration (PM_{10}). Belleudi et al. (2010) analysed the impact of particulate air pollution on ERV for respiratory diseases in Rome and reported that adjustment for PM_{10} or $PM_{2.5}$ did not alter the association of COPD with total PNC. In contrast to our results, two studies reported that after controlling for $PM_{2.5}$ associations with PNC diminished (Andersen et al. 2008; Halonen et al. 2008). Note that we only had data on PM_{10}; $PM_{2.5}$ data was not available.

Besides PNC we also analysed associations for PSC concentrations. Therefore, we converted PNC into PSCs assuming spherical particles. PSC also were adversely associated with total respiratory ERV, in agreement to Sager and Castranova (2009). We observed adverse associations between total PSCs and PSC in the size range 50 – 100 nm, 100 – 300 nm, and 300 – 1000 nm and respiratory ERV, whereas respiratory ERV increased by 3 to 9 % for an IQR increment in PSC. Effect estimates were similar for PNC and PCS. This could be expected, as we derived PSC from PNC. Nevertheless, toxicological studies support the evidence that surface area plays an important role in determining the toxicology of smaller particles because of the high potential for absorption of chemical compounds and biological interaction (Oberdörster et al. 2005). However, it is not yet possible to measure particle surface area directly on a continuous scale.

It has been proposed that UFP might play an important role in the observed health effects of particulate air pollution (Seaton 1995). In recent years, more and more epidemiological studies have used UFP as an exposure since several toxicological studies have reported cellular, pulmonary, cardiac, reproductive and other toxic effects (Ibald-Mulli et al. 2002; Valavanidis et al. 2008; Sannolo et al. 2010; Terzano et al. 2010). Interestingly, in Beijing, associations of particles < 30 nm with respiratory ERV were protective and an IQR increment in UFP with a delay of five days in PDLMs resulted in a −7 % (95 % CI: −12 % to −1 %) change in respiratory ERV. Additionally, some associations of particle fractions 30 – 50 nm and 50 – 100 nm with respiratory ERV were protective and some adverse, both being part of UFP. Overall, we did not observe consistent associations between respiratory ERV and UFP and fractions of UFP but the associations tended to be not adverse. Panel studies about the association between PEF and UFP also had problems to identify consistent findings (Pekkanen et al. 1997; Osunsanya et al. 2001). In other time-series studies adverse associations between UFP and respiratory outcomes have been reported (Andersen et al. 2008; Halonen et al. 2008). The protective associations in Beijing might be explained by the special situation of a negative correlation between small (< 30 nm) and large (> 100 nm) particles, as explained in chapter 3.1.1. Increases in sub-fractions of UFP are correlated with decreases in accumulation mode particles and vice versa. Thus, the protective association of UFP might be a result of the decreasing adverse effect of accumulation mode particles.

6.2.3.2 Respiratory mortality

For respiratory mortality all effect associations of PNC > 100 nm were adverse. Some associations of respiratory mortality for UFP and PNC < 100 nm were adverse, but not significant. Cumulative associations over four and five days were higher in magnitude than immediate associations for PNC > 100 nm and total PNC. The increase in total respiratory mortality was about 10 % for an IQR increment in $PNC_{300\text{-}1000}$ as a lagged average of four and five days and PNC_{tot} with a lag of two days.

There are only few studies that have investigated the associations with respiratory mortality for size-segregated PNC, most of which analysed effect estimates for an increase in UFP or total PNC. Findings from most of these studies suggest that PNC are adversely associated with respiratory mortality. Atkinson et al. (2010) analysed the associations between particulate air pollution and mortality in London, Great Britain; an IQR increment in total PNC (10,166 1/cm³) was associated with a 1.41 % (95 %CI: 0.48 % to 2.35 %) increase in all cause, a 2.19 % (95 % CI: 0.64 % to 3.77 %) increase in cardiovascular, and a 2.31 % (95 % CI: –0.08 % to 4.75 %) increase in respiratory deaths. We observed an increase of 9.3 % (95 % CI: 1.3 % to 17.9 %) in respiratory mortality for an IQR increment in total PNC (14,000 1/cm³), which is slightly higher in magnitude compared to the effect estimate in London. Atkinson et al. (2010) also showed that for respiratory outcomes secondary pollutants, especially non-primary $PM_{2.5}$, nitrate and sulphate were most important. This is consistent with our findings that respiratory mortality was adversely associated with total PNC and accumulation mode particles ($PNC_{300\text{-}1000}$), as accumulation mode particles were shown to mainly consist of secondary particles in Beijing (Sun et al. 2010). In Helsinki, Finland, an IQR increment in accumulation mode particles (100 – 290 nm) of the same day was also related to a 5.1 % (95 % CI: 1.2 % to 9.0 %) increase in respiratory mortality (Halonen et al. 2009). In Beijing, $PNC_{300\text{-}1000}$ showed, when compared to all other fractions, the highest correlation with NO_2 (r = 0.69), indicating that the main sources were combustion processes like traffic. Traffic-related air pollution has been shown to have a negative influence on human health (Brunekreef et al. 2009).

Accumulation mode particles (0.1 – 1 µm) contribute to 83 % of particle surface area in Beijing. Due to their high particle surface area they can adsorb more toxic substances compared to particles with less surface area. In addition, accumulation mode particles might have a diverse chemistry as they are formed by direct emission of combustion processes, coagulation of different smaller particles, and condensation of gases onto their surface (Seinfeld and Pandis 1996). Besides particle surface area, particle chemistry has been discussed to induce pathogenic effects like inflammatory injury and oxidative stress (Valavanidis et al. 2008).

Delayed concentrations of total PNC and PNC in the size range 300 – 1000 nm were adversely associated with total respiratory mortality in our single pollutant models. When controlling for other pollutants (PM_{10}, NO_2, or SO_2) effect estimates of $PNC_{300-1000}$ were lower and lost significance. In time series studies the measurement error is important when comparing effects of different pollutants (Zeger et al. 2000) and pollutants with homogenous within-city distributions will exhibit stronger associations with the outcome than pollutants with an inhomogeneous distribution (Peel et al. 2005). Concentrations of PM_{10}, NO_2, and SO_2 were measured at different sites and we thus used the regional average, and might therefore have better represented the population average exposure. However, two-pollutant models validated the effect estimate of total PNC with a lag of two days in its size and level of significance while controlling for PM_{10}, NO_2 or SO_2. This indicates that adverse associations of particle numbers with respiratory mortality were independent of particle mass. Wichmann et al (2000) also concluded that both, fine particle mass ($PM_{2.5}$) and PNC (UFP), showed independent effects on mortality in Eastern Germany.

Wichmann et al. (2000) were the first that showed that UFP is adversely associated with human mortality. In Erfurt, Germany, they analysed for a 3.5-year period (September 1995 to December 1998) associations between total mortality and particle number and mass concentration in six size classes between 0.01 µm and 2.5 µm and other air pollutants. An increment in 12,690 cm^{-3} UFP as a mean of five days was associated with an increase in mortality by 4.1 % (95 % CI: 0.1 % to 8.2 %). Whereas UFP showed the highest effect estimate with a lag of four days, strongest associations with $PM_{2.5}$ were seen on the same day of exposure. UFP showed a somewhat stronger association with mortality due to respiratory diseases compared to mortality due to cardiovascular diseases and other causes. In two further studies in Erfurt (Stölzel et al. 2007; Breitner et al. 2009) the study period was extended and results also showed, that PNC, especially for cumulative exposures of UFP and in some cases of fractions < 100 nm, were adversely associated with mortality including respiratory mortality. These findings are in contrast to our findings that show no adverse associations between respiratory mortality and UFP or PNC of fractions < 100 nm. Similar to the findings about UFP and respiratory ERV the associations between mortality and UFP might be influenced as well by the special particulate situation in Beijing with a negative relationship between large (> 100 nm) and small (< 30 nm) particles.

6.2.4 Modification of associations

We observed adverse effects of TSP on respiratory hospital admissions in Drobeta and of PNC_{tot} on respiratory mortality in Beijing, which were modified by additional factors.

6.2.4.1 Influence of air mass origin in Beijing

We showed that in Beijing air pollution including PNC has an adverse influence on respiratory mortality. Air mass history of particles - defined by back-trajectories - was used as a modifier for the associations. The information where particles come from might be a factor not only for the source but as well for other particle characteristics like chemistry. We used the NOAA "On-line Transport and Dispersion Model" (Draxler and Rolph 2003) to calculate backward trajectories of air masses with a length of 72 hours that arrive at 12:00 in Beijing. Two different approaches for the classification of air trajectories, a manual classification and classification by cluster analysis were applied. For a detailed description see Wehner et al. (2008).

The associations between PNC and respiratory mortality were elevated for stagnant and southern air masses (manual classification "local" and "south" and clusters 5-6 of cluster analysis). As an example, the increase in respiratory mortality for an increment in 10,000 cm^{-3} PNC_{tot} with a lag of two days for local air masses (manual classification) was 20.2 % (95 % CI: 2.6 % to 40.9 %) while the increase in respiratory mortality with air masses from northeast (manual classification) as well for an increase in 10,000 cm^{-3} PNC_{tot} with a lag of two was 2.1 % (95 % CI: −13.5 % to 20.5 %). The same increment in PNC resulted in a higher increase in respiratory mortality by a factor of 10 for local air masses compared to air masses from northeast. Air masses with low wind speed or even stagnant air masses spend longer times over Beijing or in the vicinity of the city, compared to air masses with high wind speed. In Beijing air pollution is a complex mixture of air pollutants and very severe (Chan and Yao 2008). Thus, particles spending longer times in polluted environments, like the air of Beijing, can accumulate condensed gases, liquids, and other particles on their existing surface and change significantly. On days with severe air pollution the Beijing urban aerosol is highly influenced by aged aerosol from the urban area and transported from the surrounding nearby industrial regions (Massling et al. 2009). In general, cleaner air masses arrive from northern directions and more polluted air masses from the south (Zhang et al. 2010). We hypothesize that the stronger effects for local air masses might be due to the chemically and physically altered particles. Supporting our hypothesis, variations in the chemical composition of $PM_{2.5}$ were found to influence the risk of hospitalizations associated with short-term exposure to $PM_{2.5}$ (Ostro et al. 2007; Bell et al. 2009). These findings need to be cautiously interpreted, as a likelihood ratio test comparing models with interaction terms to models with additive structure showed no significant differences between these two approaches. This indicated that there was only a tendency for the modification of pathogenic effects of particle concentration by air mass origin.

6.2.4.2 Influence of humidity in Drobeta

We observed adverse associations between TSP and hospital admission for chronic bronchitis in Drobeta. In addition, we analysed the modification of the significant TSP effects by the water content in the air, the absolute humidity. The adverse effect of TSP on hospital admissions for chronic bronchitis was found to be modified by air humidity. For low concentrations of TSP (< 60 $\mu g/m^3$ TSP), higher levels of humidity reduced the risk for hospital admissions but the antagonistic effect extenuated for TSP > 60 $\mu g/m^3$. As an example, for a 10 $\mu g/m^3$ TSP increment the hospital admissions for chronic bronchitis increased by 2.6 % under humid (absolute humidity = 10 g/m^3) and by 6.0 % under dry (absolute humidity = 2 g/m^3) weather conditions. An explanation of the protective effect of humidity might be that particle numbers decrease due to deliquescence assuming that inorganic salts comprise most of the ambient aerosols (Tang and Munkelwitz 1993), i.e. particles dissolve and become liquid by absorbing moisture from the air. Another explanation might be that the higher water content in the air has a positive influence on the mucociliary transport system that is an important defence mechanism and protects human airways against respiratory pathogens like particles (Chilvers and O'Callaghan 2000). For high TSP concentrations (> 60 $\mu g/m^3$) protective effects due to air humidity were not observed, which means the humidity’s antagonistic effect extenuates and high concentrations of TSP act intensively and air humidity can dispose only a fraction of them.

6.3 PNC modelling and reanalysis of associations with ERV

Measurements of size-segregated PNC are demanding and susceptible to faults which often results in missing data. In a previous study of co-workers it was shown that PNC in Beijing depend on meteorological parameters (Wu et al. 2008). Thus we used a statistical model to compute daily mean values of PNC in the size range from 3 nm to 10 µm to impute gaps in the PNC time series. These time series were later used to re-analyse the associations with respiratory ERV.

We excluded days in the modelling process and used these days for evaluation. A first graphical comparison between observed and predicted PNC showed that the two time series had similar time dependent behaviour, but the absolute concentrations might be over- or underestimated. Also, descriptive statistical parameters were similar for predicted and observed PNC. To evaluate the applicability of predicted PNC in epidemiological time series analyses - like our study design - the correlation between predicted and observed PNC is an adequate measure, as epidemiological time series analyses depend on day-to-day changes and not on the correctness of the absolute level of the predicted values (Paatero et al. 2005). In general, predicted and observed PNC were well correlated ($r > 0.7$) for fractions 3 – 10 nm, 10 – 30 nm, 3 – 100 nm (UFP), 100 – 300 nm and 300 – 1000 nm. Correlation between predicted and observed PNC of fractions in the size ranges 3 – 30 nm and 100 – 10000 nm was constant and adequate ($0.56 < r < 0.92$) throughout the year, while for the remaining fractions correlation was low for some few seasons. Thus, the use of predicted PNC, especially in the size ranges 3 – 10 nm, 10 – 30 nm 3 – 30 nm, 100 – 300 nm, and 300 – 1000 nm, is considered to be an adequate approach in epidemiological time series analyses.

As far as we know, this was the first approach to model daily mean concentrations of size-segregated PNC; thus, we cannot directly compare our results with other studies. Nevertheless, total PNC were estimated in six European cities for an epidemiological time series study using air pollutants and meteorological variables (Paatero et al. 2005), and the correlation between predicted and measured PNC was in the range 0.72 to 0.89, which is in agreement with our models with values of r in the range 0.59 to 0.85. For particle mass concentrations, non-linear models were used to forecast daily concentrations with values of the correlation coefficient of comparable magnitude to our values (Papanastasiou et al. 2007; Caselli et al. 2009).

Effect estimates of observed PNC, predicted PNC with same missing values as measured PNC, predicted PNC without missing values, and measured PNC with missing values being imputed by predicted PNC were of similar size, and the best agreement with observed PNC was for measured PNC with missing values being imputed by predicted PNC. The percentage differences of risk estimates (RR) of observed and predicted PNC were < 11 % (expect for $PNC_{30\text{-}50}$ as a mean of four days). Risk estimates of predicted and observed PNC varied most in the fractions 30 – 50 nm and 50 – 100 nm, especially for delayed associations. The tendency of associations was in most cases (85 %) identical, i.e. adverse (RR > 1) associations using predicted PNC were also adverse for observed PNC and the same for protective (RR < 1) associations.

Measures of error indicated that the use of predicted PNC in epidemiological time series analysis might be an adequate approach. Similar effect estimates of observed and predicted PNC with health impacts also indicate that it might be a reasonable approach to use imputed time series in analysing the short-term health effects with daily resolution. Both, the comparison of predicted and observed PNC and re-analysed health associations between respiratory ERV and observed as well as predicted PNC showed that the same fractions gave the best results. Altogether, this indicated that imputed time series of particle size fractions, especially in the size ranges 3 – 30 nm and 100 – 1000 nm, might be used for epidemiological assessment of short-term effects.

6.4 Final summary of results and conclusions

Particulate and gaseous air pollution was adversely associated with respiratory health in Drobeta and Beijing. In Drobeta, coarse particles (TSP) and SO_2 were adversely associated with hospital admissions for chronic bronchitis in Drobeta. Dry air aggravated the observed adverse associations. In two-pollutant models, associations of SO_2 were more consistent than of TSP indicating that sources like coal power plants and other heavy industries that are emitting SO_2 and PM were most important for the observed associations.

In Beijing, we observed adverse associations between respiratory health and PM that were size dependent. We observed similar associations for respiratory health represented by mortality and ERV due to particulate air pollution. PM_{10} showed adverse though not significant associations that are of comparable magnitude to other studies with respiratory health. PNC showed adverse association with respiratory health that were independent of particle mass (PM_{10}). For accumulation mode particles we observed the strongest adverse associations with respiratory health and the harmful effects were seen in both mortality and ERV due to respiratory diseases. The pathogen effect of accumulation mode particles was strongest for cumulative exposures of a few days. Associations of total PNC with respiratory mortality were stronger for stagnant air masses which might be an indication that altered particles and especially particle chemistry might play an important factor. Interestingly, for UFP we did not observe consistent adverse influences on respiratory health; moreover, associations tended to be protective. This might be due to the special particulate situation with negatively correlations between large and small particles and thus, protective effects of UFP being an adverse effect of larger, accumulation particles. Furthermore, NO_2 was adversely associated with respiratory ERV and SO_2 with respiratory mortality.

These findings add new information to the existing knowledge about the associations between air pollution and respiratory health, underlining the strong influence of PM and indicating size-dependent effects of particulate matter.

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Eidesstattliche Erklärung

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